

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/10579

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/135 A61K38/21 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/18395 A (PARSONS WILLIAM H ;HAJDU RICHARD (US); BERGSTROM JAMES (US); CARD) 7 March 2002 (2002-03-07) cited in the application page 10, lines 3-10	1-13
Y	EP 1 002 792 A (YOSHITOMI PHARMACEUTICAL) 24 May 2000 (2000-05-24) cited in the application page 18, paragraph 167 - page 19, paragraph 174	1-13
Y	WO 02/072019 A (PARKER SUEZANNE E ;VICAL INC (US); HORTON HOLLY M (US)) 19 September 2002 (2002-09-19) page 1 - page 5	1-13
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

9 December 2003

Date of mailing of the international search report

12 03. 2004

Name and mailing address of the ISA

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Deck, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	DE 197 39 693 A (SCHERING AG) 11 March 1999 (1999-03-11) the whole document	1-13
Y	BRINKMANN VOLKER ET AL: "The immune modulator FTY720 targets sphingosine 1-phosphate receptors" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 24, 14 June 2002 (2002-06-14), pages 21453-21457, XP002264445 ISSN: 0021-9258 page 21457	1-13
Y	BRINKMANN V ET AL: "FTY720: targeting G-protein-coupled receptors for sphingosine 1-phosphate in transplantation and autoimmunity" CURRENT OPINION IN IMMUNOLOGY, CURRENT BIOLOGY LTD, XX, vol. 14, no. 5, 19 July 2002 (2002-07-19), pages 569-575, XP004377409 ISSN: 0952-7915 page 570, last paragraph - page 571, paragraph 1	1-13
Y	MOSER HUGO W: "Clinical and therapeutic aspects of adrenoleukodystrophy and adrenomyeloneuropathy" JOURNAL OF NEUROPATHOLOGY AND EXPERIMENTAL NEUROLOGY, vol. 54, no. 5, 1995, pages 740-745, XP009022840 ISSN: 0022-3069 page 743, last paragraph	1-13
Y	HOSHINO Y ET AL: "FTY720, a novel immunosuppressant, shows a synergistic effect in combination with FK 506 in rat allograft models" TRANSPLANTATION PROCEEDINGS, vol. 31, no. 1-2, February 1999 (1999-02), pages 1224-1226, XP002264446 XVIIth World Congress of the Transplantation Society; Montreal, Quebec, Canada; July 12-17, 1998 ISSN: 0041-1345 the whole document	1-5,11

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 6-10 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-4, 6-8, 11-13 (partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-13 (part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4, 6-8, 11-13 (partially)

Present claims 1-4, 6-8, 11-13 relate to an extremely large number of possible compounds (51P receptor agonists). In fact, the claims contain so many options, variables, possible permutations and provisos that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely for the compounds recited in claims 5 and 9 and disclosed in the description, pp. 11-12 and for the general concept of 51P receptor agonist.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an interferon; uses thereof in the treatment of a demyelinating disease.

2. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an altered peptide ligand; uses thereof in the treatment of a demyelinating disease.

3. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an immunosuppressant; uses thereof in the treatment of a demyelinating disease.

4. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an adenosine deaminase inhibitor; uses thereof in the treatment of a demyelinating disease.

5. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is IV immunoglobulin G; uses thereof in the treatment of a demyelinating disease.

6. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is a monoclonal antibody to a T-cell surface marker; uses thereof in the treatment of a demyelinating disease.

7. claims: 1-13 (part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is a TH2 promoting cytokine; uses thereof in the treatment of a demyelinating disease.

8. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is a compound which inhibits expression of TH1 promoting cytokines; uses thereof in the treatment of a demyelinating disease.

9. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an antispasticity agent; uses thereof in the treatment of a demyelinating disease.

10. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an AMPA glutamate receptor agonist; uses thereof in the treatment of a demyelinating disease.

11. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an inhibitor of VCAM-1 expression or an antagonist of its ligand; uses thereof in the treatment of a demyelinating disease.

12. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is an anti-macrophage migration inhibitory factor; uses thereof in the treatment of a demyelinating disease.

13. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is a cathepsin S inhibitor; uses thereof in the treatment of a demyelinating disease.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

14. claims: 1-13 (part)

Pharmaceutical compositions comprising a sphingosine-1-phosphate receptor agonist and a co-agent which is a mTOR inhibitor; uses thereof in the treatment of a demyelinating disease.

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International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0218395	A	07-03-2002	AU 8533101 A	13-03-2002
			CA 2421893 A1	07-03-2002
			EP 1315735 A1	04-06-2003
			WO 0218395 A1	07-03-2002
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			AU 6523098 A	30-10-1998
			BR 9808481 A	23-05-2000
			CA 2286315 A1	15-10-1998
			EP 1002792 A1	24-05-2000
			IL 132208 A	31-07-2003
			NZ 500713 A	28-07-2000
			US 6214873 B1	10-04-2001
			CN 1137086 C	04-02-2004
			EP 1319651 A2	18-06-2003
			WO 9845249 A1	15-10-1998
			RU 2198162 C2	10-02-2003

WO 02072019	A	19-09-2002	WO 02072019 A2	19-09-2002
			US 2003091544 A1	15-05-2003

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